How common is malnutrition among patients with liver disease?

Malnutrition is quite common in this population. The reported prevalence rates vary considerably depending on the assessment tool used to define malnutrition and the type of patient population that was studied (ie, hospitalized patients versus outpatients). Many studies have reported rates on the order of 65–90%, and studies have consistently reported that the prevalence of malnutrition increases as the patient's disease progresses. Even among patients with Child-Pugh class A cirrhosis, malnutrition rates may be as high as 20%.

Why does malnutrition occur in these patients?

A number of variables contribute to malnutrition in patients with cirrhosis. First, malnutrition in this population is often related to poor dietary intake, which can occur for a variety of reasons: Prescribed diets, in particular sodium-restricted diets, are less palatable to patients, and patients with large ascites often experience early satiety. Rates of anorexia or diminished appetite are also higher in patients with liver disease, particularly in the setting of acute decompensation or acute illness. Some of the medications prescribed to these patients—for example, lactulose—may cause increased gas, bloating, and diarrhea. Finally, the presence of significant encephalopathy may impair dietary intake, and socioeconomic barriers may limit a patient's access to good nutrition and/or assistance in preparing and taking meals.

In addition to poor intake, patients with chronic liver disease also demonstrate variable amounts of either maldigestion or malabsorption, which may be related to cholestasis, small bowel bacterial overgrowth, and/or pancreatic insufficiency. Nutrients may also bypass the liver altogether in patients with significant portosystemic shunting. Finally, altered glucose homeostasis in patients with chronic liver disease can contribute to malnutrition, and, as in other patients, hypermetabolism and catabolism are seen with severe acute illness.

How does the presence of cirrhosis affect a patient's nutritional status?

One reason for this association is that normal glycogen stores in the liver become depleted in patients with cirrhosis. During an overnight fasting period, the rate of liver glycogenolysis is significantly lower in cirrhotic patients compared to controls, whereas the relative contribution of gluconeogenesis to glucose production is much greater in patients with cirrhosis compared to controls. This difference likely contributes to accelerated muscle loss among cirrhotic patients.

Resting metabolic rate may be another factor that alters nutritional status in patients with cirrhosis, although data in this area are conflicting. Regardless, a subset of patients probably has alterations in their resting metabolic rate, and energy and protein requirements are certainly increased in the setting of acute illness and hospitalization.

What challenges do clinicians face when assessing nutritional status in patients with liver disease?

First, nutrition training in gastroenterology programs is not always sufficient, so many clinicians may...
lack the level of understanding needed to properly treat patients with significant nutritional problems. Second, the nutritional assessments that are familiar to most clinicians—such as body mass index (BMI) and serum protein tests—are less accurate and/or less reliable in patients with cirrhosis. Third, access to a registered dietitian who can assist in the assessment and care of liver disease patients is often limited in hepatology clinics (outside of liver transplantation clinics where the presence of registered dietitians is mandated). Finally, gastroenterologists and hepatologists sometimes must overcome misinformation about proper nutrition provided to patients with cirrhosis. For example, older data suggested that patients with hepatic encephalopathy needed a low-protein diet, while contemporary research has shown that patients with hepatic encephalopathy actually need increased protein in their diet. Unfortunately, not all clinicians are aware of this change in dietary guidelines. Thus, when patients are referred to a hepatology clinic, they sometimes need to be re-educated about their nutritional requirements.

**G&H** What types of assessments can be used to evaluate the nutritional status of patients with liver disease?

**HMP** A variety of assessments can be used to evaluate patients’ nutritional status. Anthropometric tools include BMI, midarm muscle circumference, and triceps skinfold thickness. Radiographic examinations can be used to provide information about muscle bulk and/or subcutaneous or central fat stores. Functional tests—such as hand-grip strength—can assess muscle strength as a marker of muscle tone. Finally, global assessment tools, which are typically in the format of flow charts or algorithms, can integrate information about patients’ dietary intake and how their weight has changed in recent weeks and months; some global assessment tools also include additional variables such as anthropometric measurements.

**G&H** What are some of the advantages and disadvantages of these tools for assessing patients with chronic liver disease?

**HMP** The advantages of serum protein measurements are their ease of measurement and objectively reported results. However, because albumin synthesis can be impaired in patients with chronic liver disease, this marker is not fully reflective of patients’ nutritional state. Prealbumin levels can still be informative because of this protein’s shorter half-life. In particular, measurement of prealbumin can help clinicians judge the efficacy of a nutritional intervention.

BMI is probably the most widely utilized nutritional assessment tool in the general population and thus is familiar to most clinicians; however, its utility is limited in the setting of cirrhosis because standard BMI cutoffs are inaccurate in patients who have significant volume overload, especially ascites; this inaccuracy could cause clinicians to overestimate the nutritional status of patients with liver disease. To address this problem, a study was conducted several years ago to assess BMI and other measures of nutrition in patients with volume overload, and the authors of this study proposed altered BMI cutoff values for underweight patients with cirrhosis; specifically, they proposed adding an adjustment factor based on whether the patient has no ascites, mild ascites, or large ascites. While estimating the contribution of ascites may be vulnerable to error, this adjusted BMI can be used if clinicians lack the expertise or support to administer other nutritional assessment tools.

Other anthropometric tools that do not require adjustment (and thus may be more accurate in cirrhotic patients) include measurements of midarm muscle circumference and triceps skinfold thickness. A measure of muscle bulk, midarm muscle circumference can be compared against normative values for the healthy population, and malnutrition as measured by midarm muscle circumference has been shown to be associated with the risk of mortality in patients with cirrhosis. Triceps skinfold thickness is also predictive of mortality in patients with cirrhosis; this measurement assesses subcutaneous adipose tissue and is relatively easy to perform.

In terms of functional assessment tools, hand-grip strength can be readily used to assess nutritional status; a dynamometer is used to measure grip strength, and this measurement can be compared against normative values for a control group that is matched by age and gender. Data suggest that hand-grip strength might be more sensitive than some of the global assessment tools for detecting malnutrition in patients with cirrhosis; specifically, hand-grip strength may be better able to predict malnutrition-related outcomes at 1 year.

Regarding the use of cross-sectional imaging to assess nutrition, a number of studies in the past couple of years have used imaging to examine sarcopenia. Patients with liver disease frequently undergo computed tomography and magnetic resonance imaging as part of their liver cancer surveillance, so imaging data are often available and may be used to measure muscle bulk. However, it is not yet clear how such information can be used on an individual patient basis.

Finally, global assessment tools can also be used to assess nutritional status in patients with liver disease. The Subjective Global Assessment is probably the most well-known such tool for assessing the general patient population. There are also global assessment tools.
designed specifically for patients with liver disease, such as the one developed at the Royal Free Hospital, and these tools are a fairly simple way to assess nutritional status in patients with cirrhosis.

G&H Which of these tools is preferred for the assessment of patients with liver disease?

HMP This decision largely depends on the resources available in a given clinic. I work with a registered dietitian in liver transplantation clinic, so I prefer to collect data on hand-grip strength, as this measure can be fairly dynamic. Anecdotally, I find that hand-grip strength will improve over the course of weeks to months as a nutritional intervention takes effect. Global assessment tools can also be fairly informative, despite being relatively simple.

G&H When is nutritional supplementation necessary for patients with liver disease?

HMP Nutritional supplementation is necessary whenever patients are unable to meet their nutritional requirements through their regular diet. Patients often overestimate how well they are doing with their nutrition, so performing careful nutritional interviews is quite helpful; calorie and protein accounting can also be performed in hospitalized patients. If the clinician can show patients that they are only taking 20–30% of their nutritional requirement, then they may be more receptive to using supplements.

Inpatients often have particular difficulty meeting their nutritional needs—even with the use of volitional supplements such as Ensure (Abbott), Glucerna (Abbott), or Boost (Nestle)—because calorie and protein requirements can increase dramatically with the added insult of an acute illness. In these cases, I usually recommend enteric tube feeding. Parenteral supplementation may be required in addition to enteral nutrition if patients have particularly high nutritional requirements or if their enteral feeds are poorly tolerated or frequently interrupted.

G&H Are specific diets recommended for patients with liver disease?

HMP Guidelines regarding proper diets for patients with cirrhosis come from the European Society for Clinical Nutrition and Metabolism. In 2009, this organization published guidelines specifically addressing patients with liver disease; these guidelines advise that patients with liver disease consume 35–40 kcals/kg/day, with a protein intake of 1.2–1.5 g/kg/day. Other data that inform my dietary recommendations come from a 2008 study by Plank and colleagues; in this study, approximately 100 patients with cirrhosis were provided with nutritional supplementation over a 12-month period. All of the patients were given 2 cans of Ensure Plus (Abbott), which collectively provided approximately 700 calories and 25 g of protein, but the timing of the supplementation differed between the 2 study groups. One group of patients was randomized to take the supplements during the evening or nighttime hours, while the other group was randomized to take the supplement during morning and daytime hours. Patients assigned to nocturnal supplementation achieved significantly greater increases in total body protein stores, as shown by a 2-kg increase in lean muscle tissue, which I believe is likely related to these patients’ alteration in glucose homeostasis. Given this finding, I strongly recommend that both outpatients and hospitalized patients have an evening snack. For hospitalized patients who require enteral nutrition support and are able to eat during the daytime, the tube feed supplementation should be provided during the nighttime hours.

G&H How does improving nutritional status lead to better liver disease outcomes?

HMP There is a strong body of literature demonstrating that malnutrition contributes to poor outcomes; however, fewer studies have tested the widely held belief that nutritional supplementation will improve clinical outcomes. In 1 study that did assess the impact of nutritional supplementation on patients with cirrhosis (mostly patients with Child-Pugh class A cirrhosis), differences were observed in terms of both complications and mortality at 1 year. Among patients who did not receive nutrition supplementation, the mortality rate at 1 year was 20%; no deaths occurred in the subset of patients who were provided with supplemental nutrition during the 12-month study period. Similarly, the rate of complications among patients who were not given nutritional supplementation was much higher than the rate of complications among patients who did receive nutritional supplementation (65% vs 11%). Given the significant benefit in this study for patients with relatively early disease (Child-Pugh class A cirrhosis), there is likely greater benefit to be seen in patients with more advanced disease. (However, there are ethical limitations to the type of nutritional intervention studies that may be performed.)

G&H What further research would you like to see in this area?

HMP First, better data are needed to determine which nutritional assessment tools to use in patients with liver disease and whether different tools are needed for clinic patients versus inpatients. Additionally, as I just men-
tioned, there is a need for well-designed trials that can determine whether nutritional intervention improves various outcomes of interest, such as mortality rates, transplantation outcomes, complications, hospitalization rate, and hospital length of stay.

Studies are also needed to determine whether the presence of a registered dietician in the hepatology clinic setting impacts patient outcomes. Anecdotally, I feel that having access to a registered dietitian improves outcomes in liver disease patients; if studies could demonstrate that the presence of a registered dietitian does indeed improve outcomes and reduce hospitalizations, then such data could help to justify the cost of having such resources available to outpatients.

Finally, although clinicians often interfere with hospitalized patients’ nutrition by keeping them NPO (nil per os) or interrupting tube feeds for tests and procedures, many clinicians remain concerned about the risk of using parenteral nutrition in the sickest subset of patients with cirrhosis. Thus, data are needed to clarify the risks and benefits of parenteral nutrition in this population, and guidelines are needed to clarify when such nutritional support is appropriate.

**Suggested Reading**